

Professor Hamish McCallum  
University of Tasmania  
Hobart  
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27<sup>th</sup> February 2008

Dear Professor McCallum

### **Opinion on a chemical aetiology for Facial tumor development in the Tasmanian Devil**

Thank you for asking me to provide an toxicological opinion on the data set that you have generated from analysis in Tasmanian devil tissues of metals, pesticides and toxic organic compounds.

This opinion is provided in relationship to the data set that you have sent to me and takes into account our discussions on the background to devil behaviour and the spread of the facial cancer in this species. In support of my opinion I enclose a copy of my curriculum vitae.(encl.)

I would first of all emphasise that the numbers of animals evaluated is relatively small in respect of the different types of habitat and consequentially toxicological exposures that might be involved. Consideration of the geographical location of the animals studied provides no clues to potential chemical aetiology. There is no common factor which would separate the diseased devils from the disease-free devils. The geographical locations merely show that one is more likely to find diseased devils on the east coast and that there is a substantial overlap between the diseased and disease-free devils in the centre of Tasmania from North to South (see map below). Analysis of dioxins and PBDEs has been carried out in the premier laboratory for this purpose in Australia, the National Measurement Institute which has the benefit of highly experienced scientists and works under NATA accreditation. Other analyses were carried out in the NATA accredited laboratory, Analytical Services Tasmania and 1080 measurements by the Department of Primary Industries and Fisheries in Queensland. I consider that the figures provided on dioxins (PCDD and PCDF), pesticides and 1080 (Fluoro-acetate) are reliable as are the measurements of metals.



I was unable to see any consistent patterns of variations in the various dioxin/furan congeners. As expected the congener patterns were dominated by the presence of octachlorodibenzodioxin. The same applies to the measurements of polybrominated diphenyl ethers. I noted Bob Symon's comment that he found high levels of hexabromobiphenyl (BB 153) but am unsure how to interpret that, other than to note that these concentrations are less than the NOEL (see below). Similarly the elevations in decabromo-diphenyl ether 209 (BDE 209) is interesting but unrelated to the presence of cancer. The range of concentrations of these was substantial -- for BB 153; 330 to 10,400 pg/g lipid and for BDE 209; less than 90 to 7520 pg/g lipid ( I do not have any conversion of pg/g lipid to pg/kg body weight in devils). The measurements of the various pesticides that have been examined are only remarkable in that they are invariably below the limit of detection. The same applies to measurements of fluoro-acetate (1080) which was also undetectable. The concentrations of all metals, arsenic cadmium lead and mercury are equally unremarkable. Of these, only arsenic is likely to be associated with the development of cancer and the concentrations are generally low with a range of between 0.3 to 0.7 mg per kilogram WMB and no pattern of excess.

The WHO IPCS (EHC) review in 1994 concluded that polybrominated biphenyls are extremely persistent in living organisms and produce chronic toxic effects and cancer in animals. Though the acute toxicity was low, cancer was induced at a dose of 500,000 pg/kg body weight per day. The no-observed-effect level (NOEL) was 150,000 pg/kg body weight per day. The International Agency for Research on Cancer (IARC) has classified hexabromobiphenyl as a possible human carcinogen (IARC group 2B). (Environmental Health Criteria (EHC) 152: Polybrominated biphenyls. IPCS International Programme on chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1994.)

Decabromodiphenyl ether (BDE 209), the most highly brominated of the polybrominated diphenyl ethers is the world's most widely used brominated flame retardant. It is used in hard plastic electronic consumer products and in flame-retarded textiles for furniture. Several international organizations risk assessments have found BDE209 to be safe in its' current use. BDE 209 underwent an evaluation under the Voluntary Children's Chemical Evaluation Program (VCCEP) of US EPA and was found to pose negligible health risks for children. There was in particular no evidence of carcinogenicity in 'in vitro' or in animal studies using as much as 2550 mg/kg/day in rats and 6650mg/kg/day in mice. The concentrations of these two compounds are the highest of all the measures taken in the devils but do not appear to show any relationship to the development of cancer.

The evaluations of the differences that might occur between these various measures have been divided into those animals that have been found to have cancer against those that did not have cancer. I have tried to establish whether there are any reasonable geographical associations but have been limited because of the lack of detailed information on likely environmental exposures of the animals who did and did not have cancer. Again the numbers are too small. An alternative means of separation of the groups would have been to do so on a geographical basis utilising the boundaries of cancer-linked area with areas in which cancer had not been found. However this approach is also flawed because it could not take into account focii of rural contamination compared with larger areas of urban and suburban contamination. Since the Devil does act as a scavenger is likely that in circumstances where they are living proximal to human habitation, be it in urban or rural environments, they would be likely to have exposure to a whole range of human waste

products including microbiological and chemical wastes.

The pattern of spread of the disease is not consistent with a chemical aetiology. There is no identified focus of chemical exposure or concurrent spread of chemical exposure from the north-east of Tasmania. Indeed the rate of spread of cancer from the north-east of Tasmania is relatively slow at around 5 to 10 km per year (based on studies in Freycinet peninsula where good baseline data were available). This relatively slow transmission of the disease is consistent with either contagious disease or animal to animal contact in which the transmission is fortuitously, inefficient. This pattern does not provide any reasonable fit to any known or as yet unidentified chemical exposure.

The development of this cancer seems to be the product of a 'de-novo' transmissible cell line. The origins of this cell line are obscure. It could, putatively have been associated with initiation by chemical or radiochemical exposure in the first instance. There is however no evidence that this is the case. At this point in time is highly unlikely that any primary event would be able to be identified. It is now 12 years since the disease was first detected in 1996 in north-east Tasmania. There is no specific unusual characteristic in that region which would account for excessive exposure to any specific chemicals. The lack of measurable concentrations of pesticides or fluoro-acetate at present suggests that there has not been over-exposure to chemicals used in agriculture or forestry.

Chemical exposures might account for suppression of immune function and perpetuation of cancerous cell lines. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is immunosuppressive. In the immune system, the T-cell lineage and B-cell lineages are particularly affected by dioxins. TCDD-exposed mice had a significantly higher titre of IgM compared to controls. Similarly Harbor porpoises from the North and Baltic Seas exhibit a higher incidence of bacterial infections compared to whales from less polluted arctic waters. Analysis revealed an association between elevated body burdens of environmental contaminants, such as polychlorinated biphenyls (PCB) and polybrominated diphenyl ether (PBDE) and lymphoid depletion in thymus and spleen of these whales. An investigation of changes of blood cytokine mRNA levels in healthy and diseased harbor porpoises showed a marked up-regulation of IL-10 in severely diseased whales, with evidence of chronic bacterial infections. Environmental exposure to polybrominated diphenyl ethers (PBDEs) causes immunomodulation in captive nestling American kestrels. Body burden concentrations 120x higher in the treated birds than controls resulted in greater T-cell-mediated immunity, which was negatively associated with increasing BDE-47 concentrations.. Immunomodulation from PBDE exposure is thus present at these relatively high levels of exposure. These findings are congruent with weakening of the immune system by relatively high concentrations of PCDDs and PBDEs. However the current concentrations measured in the devils are so low that they would not be expected to have this characteristic. Further study of this is warranted.

Tasmanian devils are known to be prone to the development of various cancers. This accounts for the relatively tardy identification of the facial cancer. It might be argued that this might make the Tasmanian Devil especially susceptible to chemical carcinogenesis at relatively low concentrations of any suspect compound. As things stand at present no such carcinogen has been identified at a concentration approaching that likely to be carcinogenic. However the propensity for devils to develop cancer is suggestive of potential genetic origins and the potential for some chemical to act on oncogenes in this species. This view is however speculative and unsupported by any of the chemical measurements made to date.

In the understanding of the natural history of this disease there is a need to keep an open mind on its genesis whether it be mono- or multifactorial. My opinion is that a primary chemical aetiology is unlikely. Chemical exposure may contribute to disease development but no evidence, as yet provided, would identify any one compound likely to fit this role. It

is my view that the possibility of a chemical exposure contribution cannot be totally excluded but that the pattern of disease would suggest otherwise and that the causative factor(s) should be sought elsewhere such as in the direct transfer of cell by bite, already enunciated.

I hope this will be of assistance in your deliberations

Michael R. Moore

Encl. CV

## MICHAEL R. MOORE

*Director, National Research Centre for Environmental Toxicology, (EnTox.)  
Professor of Medicine, The University of Queensland ,  
Adjunct Professor of Public Health, Griffith University,  
Adjunct Professor in Faculty of Science, University of the Sunshine Coast.  
Adjunct Professor in Public Health, Queensland University of Technology  
CoDirector Australian Centres for Human Health Risk Assessment*

Michael Moore is Director of The National Research Centre for Environmental Toxicology. He holds the position of Professor in Medicine at the University of Queensland, Adjunct Professor of Public Health in Griffith University, Adjunct Professor in Queensland University of Technology and Adjunct Professor in the Faculty of Science, Sunshine Coast University. He is a registered Toxicologist, (Eurotox & Institute of Biology, United Kingdom), Founder Council Member and Registrar of the Australasian College of Toxicology and Risk Assessment (ACTRA), possesses a PhD in Medicine and was awarded a Doctorate in Science in the field of biochemistry in medicine. He has trained in Clinical Pharmacology in the Royal Postgraduate Medical School in London. He is a director of the Australian Centres for Human Health Risk Assessment. Michael worked previously in the University of Glasgow, where he was Reader in Medicine and Therapeutics. He was a director of Monklands and Bellshill NHS Hospital Trust in Scotland and Justice of the Peace. Michael has written several books and numerous book chapters and over 500 research publications. His fields of interest include the toxicology of metals, risk assessment, air quality, alcoholism, cyanobacteria and disorders of porphyrin metabolism.

### EDUCATION

UNIVERSITY OF GLASGOW  
*B.Sc., Honours, Biochemistry, 1967;  
Ph.D., Medicine, 1971  
D.Sc., Biochemistry in Medicine 1987*

### EXPERIENCE

- THE UNIVERSITY OF QUEENSLAND
  - *Professor of Medicine 1994 -*
- GRIFFITH UNIVERSITY, QUEENSLAND
  - *Adjunct Professor of Public Health 1995 -*
- QUEENSLAND HEALTH
  - *Director of Queensland Health Scientific Services 1998 – 2005*
- UNIVERSITY OF CAPE TOWN
  - *Honorary Lecturer 2000 - 2005*
- University of the Sunshine Coast
  - *Adjunct Professor in Faculty of Science 2002-*
- Queensland University of Technology
  - *Adjunct Professor in Health Sciences 2004 -*
- LANARKSHIRE HEALTH BOARD
  - *Non-executive Director, 1992 - 1994 Monklands & Bellshill Hospitals NHS Trust (Responsibility for Community Relations and Laboratory Services)*
- THE ROYAL SOCIETY / CONICET

- *Visiting Fellow to Argentina 1992* Study tour to Buenos Aires, Rosario, Bahia Blanca, Mar del Plata, Cordoba, La Huerta Grande, Iguasu, San Carlos de Bariloche. – Appointed, Miembro Academia de Ciencias Medicas de Cordoba (MACM).
- UNIVERSITY OF GLASGOW
  - *Reader Senior Lecturer, and Lecturer 1975 to 1994 in Materia Medica, Medicine and Medicine & Therapeutics; (Elected to Senatus Academicus 1984)*
- ROYAL POSTGRADUATE MEDICAL SCHOOL,
  - *Training in Clinical Pharmacology 1986*
- UNIVERSITY OF CAPE TOWN
  - *Research Fellow and Senior Research Fellow SA MRC/NMR Porphyrias Unit , Groote Schuur Hospital Cape Town 1982-3, 1992 & 1996; Research in the Porphyrias and Lead and other metal exposures*
- GLASGOW CALEDONIAN UNIVERSITY/ GLASGOW POLYTECHNIC
  - *Senior Specialist Lecturer 1982 - 1994 Teaching in Metabolic Diseases, Toxicology, Biochemistry & Haematology*
- UNIVERSITY OF GLASGOW
  - *Research Fellow and Research Assistant 1967 to 1975, Departments of Medicine and Materia Medica, Research in Iron & Porphyrin Metabolism, Alcoholism and Metal Toxicology.*

## TRACK RECORD

Michael Moore is a registered Toxicologist (BTS & Eurotox) Member and Registrar of ACTRA and has trained in Clinical Pharmacology.

- Elected Council Member – Registrar, Australasian College of Toxicology and Risk Assessment - 2007
- Advisory Board Member Australian Pesticides and Veterinary Medicines Authority 2007 –
- Advisory Council Member, Australian Centre for Tropical Freshwater Research, James Cook University. 2007-
- Member Steering Committee, Queensland Health Hospital Wastewater Characterisation Project 2007 –
- Member Rio Tinto Corporate Crisis Committee 2008 -
- Chair, NHMRC, Air Quality In and Around Traffic Tunnels Working Committee 2007
- Member Queensland Government Marine Stinger Advisory Committee 2007 -
- Member; Australian Drug Evaluations Committee 2003 -
- Member of the National Drugs and Poisons Schedules Committee (TGA) 1999 –
- Expert advisor; Queensland EPA; Remediation of Narangba contaminated site 2006 –
- Expert Advisor - Toowoomba City Council; Waste water reuse strategy. 2006
- Queensland Health Water working Group – Environmental Health. 2006 -
- Member DVA Scientific Advisory Group Centre for Military and Veteran Health 2005 –
- Member NSW Food Authority Dioxins Expert Panel 2005 - 2007
- Member, NHMRC Working Group on Toxicity & Risk Assessment 2002 - 2005
- Chair, NHMRC Drinking Water Treatment Chemicals Working Party. 2000 - 2005
- Member of the Health and Medical Research Council for Queensland, 2001- 2004
- Member External Advisory Group – Institute for Health and Environmental Studies – University of the Sunshine Coast 2003 -
- Chair: Research, Development and Training Committee of QHPSS 2000 - 2005
- Member QIMR Clinical Trial Protocol Committee – 2005 -
- Member Science Program Advisory committee University of the Sunshine Coast 2002 -
- Member of the Technical advisory committee of Environment Australia's Air Toxics forum: 1999 - 2003
- Member Environment Australia, National Dioxins consultative Group 2001- 2004
- Expert Advisor; Stuart Facilitation Working Group, Dept of State Development.2001-2004
- Member DHAC report on health impacts of Indoor Air Quality, 2000
- Member Department of Veterans Affairs, Korean Veterans Mortality Study advisory committee 1998 - 2005;
- Member Department of Veterans Affairs, Korean Veterans Health Study advisory committee 2001 - 2005;
- Member Scientific Advisory committee Study of Health Outcomes in Aircraft Maintenance Personnel, 2000 - 2006
- Member DVA expert committee; Depleted uranium Exposure and the ADF 2001-2002
- Member of IPCS Task Groups on Lead 1993-1994; Nitrogen Oxides 1994; Aluminium 1995, Copper 1996, Zinc 1996, Essential Trace elements 1998 & Arsenic 1999:
- Chairman of the Community And Environmental Health Advisory Panel of the Minerals Council of Australia 1999 - 2005:
- Member: International Council on Mining & Metals Health Advisory Panel:
- Australian representative - WHO expert panel on Health effects of Dioxin exposure 1999
- Member enHealth working party on Environmental Health Risk Assessment, 1998.
- Chair; Environmental Health Risk Assessment course QCPH, 1997
- Member of the Advisory Committee of the Centre for Environment and Population Health (Griffith University)

- Expert Advisor; NHMRC Dental Amalgam and mercury in dentistry working party 1998
- Member NSW ETS Standards Committee 1998
- Member Australian (NHMRC) Lead abatement evaluation steering committee 1997.
- Member: PACIA Community Advisory Panel 2002 - 2005
- Member Blue green Algae Task Force (Queensland) 1995-
- Member National Cyanobacterial Toxin Guidelines Working Group. 1996-.
- Expert Advisor NHMRC working party on carcinogenic soil contaminants. 1995 - 2000
- Member Queensland Government Irukandji Task Force 2002 – 2007
- Member NH&MRC, Environmental Health & Nutrition Standing Committee (Toxicology Adviser) 1994–1997.
- Advisor to IPCS/ WHO; on Lead 1992 - 1994,
- Council member, Australasian Society for Clinical and Experimental Pharmacology and Toxicology (ASCEPT) 1997 - 1999
- Past Convener of the Toxicology section of ASCEPT.
- Chairman of the Local organising committee of the International Congress of Toxicology-IX,- Brisbane 2001.
- Trustee - The Porphyrias Charitable Trust (UK) 1989
- Reviewer for numerous journals; Nature, The Lancet, British Medical Journal, New Scientist, Clinical Science, Clin. Chim. Acta, Biochemical Journal, British Journal of Dermatology, etc.
- Extramural appointments as: Justice of the Peace (Cumbernauld & Kilsyth) 1992 -; Rotarian in Kilsyth Scotland (President 1993) and in Salisbury, district 9630 Queensland. 1994 - Archivist District 1020, 1993 - 1994, Paul Harris Fellow 1998; Chairman, Lanarkshire Health Council 1991 – 1993; Chairman Kilsyth Community Council 1984 - 1994 - Editor of '*The Kilsythian*' 1984 – 1990; Chairman, Kilsyth Academy School Board 1992 - 1994, Member from 1989; Vice Chairman & Member, Kilsyth Crime Prevention Panel, 1987 – 1994; President, Hetherington House - Postgraduate Students Club - 1968 – 1970; Hon. FP Secretary, Alchemists Club 1965 – 1966; Sporting interests in climbing & walking; Cycling; Yachting; Motor sport (member of MGCC , Morgan SCC), Western Pedal Power Association); Director & Company Secretary, Clock Theatre Kilsyth Ltd. 1975 to 1994.
- Convener of Training Committee - Scottish Association of Health Councils 1991- 1994
- Editor - Molecular Aspects of Medicine and International Journal of Toxicology, Occupational & Environmental Health.
- Research Grants held from 1971 from, MRC(UK), SAMRC, NH&MRC, SHHD, CEC, SHERT, ARC, NATO, Nuffield Foundation, Wellcome Foundation, Watson Foundation, CONICET, GGHB, SEQWB.
- Fellowships from; The Royal Society, The Gordon Conferences, P.G. Unna Stiftung, British Council (to Eastern Europe), Graham Wilson Fund
- Industrial Consultancies from; ICI, The Cookson Group, Wedgwood, Royal Doulton, Combe Inc., Servier, Estée Lauder, Hutumaki Oy, Associated Octel, MIM Holdings, Dow-Elanco. SPPM, Cochlear, Pasminco

Member of: The Biochemical Society; British Inherited Metabolic Diseases Group; Tetrapyrrole Discussion Group; African Society for the Study of the Liver ; Australasian Society for Clinical & Experimental Pharmacology & Toxicology; Australasian Ecotoxicological Society, British Toxicological Society. Michael has written several books and numerous book chapters and over 400 research publications. His fields of interest include the toxicology of metals, alcoholism, cyanobacteria and disorders of porphyrin metabolism.

## BOOKS, BOOK Chapters & REPORTS

- THE PORPHYRIAS Clinics in Haematology 9 Eds. A. Goldberg and M.R. Moore Pub. Saunders, London, 1980.
- PORPHYRIA Clinics in Dermatology eds. P.B. Disler and M.R. Moore, Pub. Lippincott, Philadelphia, 1985.
- PORPHYRIA AND YOU R.S. Day and M.R. Moore Pub. Dept. of Health & Welfare, Pretoria, 1985.
- THE LEAD DEBATE: The Environment, Toxicology and Child Health. M.R. Moore with eds R. Lansdown and W. Yuill. Pub. Croom Helm, London and Sydney, 1986.
- DISORDERS OF PORPHYRIN METABOLISM M.R. Moore, K.E.L. McColl, C. Rimington and Sir A. Goldberg, Pub. Plenum Press, New York, 1987.
- PORPHYRIA, DRUG LISTS M.R. Moore and K.E.L. McColl University of Glasgow, Hunterprint Cumbernauld. Editions in 1984, 1985, 1987, 1988, 1991 and 1994
- A CENTURY OF PORPHYRIA Molecular Aspects of Medicine Ed. M.R. Moore Pergamon Press, London. 1990
- ALUMINIUM: Report of an International Meeting. National Environmental Health Forum Monographs. Metal Series No 1 eds. P. Imray, M.R. Moore P.W. Callan & W.H. Lock. South Australian Health Commission, Glenelg Press pp 1-3 1996 (ISBN 0 642 25881 3)
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- BIOAVAILABILITY OF MATERIALS FROM CONTAMINATED SOILS. Moore, M.R. In: The Health Risk Assessment and Management of Contaminated Sites. Eds: A. Langley, B. Markey and H. Hill. Commonwealth Department of Human Services and Health and the Environmental Protection Agency. Contaminated Sites Monograph Series No. 5 South Australian Health Commission, 339-353 (1996).
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- IMPACT OF CLIMATE CHANGE ON TOXIC CYANOBACTERIAL (BLUE-GREEN ALGAL) BLOOMS AND ALGAL TOXIN PRODUCTION IN QUEENSLAND. Garnett, C., Shaw, G., Moore, D., Florian, P., & Moore M. B010898 Dept of Natural Resources & Mines Brisbane March 2003
- INVESTIGATION OF CHANGES IN CELL CYCLE DISTRIBUTION IN CULTURED HEPG<sub>2</sub> CELLS WITH PECTENOTOXINS-2 SECO ACIDS Burgess, V., Zhang, Y., Eaglesham, G., Tzang, C.H., Yang, Z., Shaw, G., Lam, P.K.S., Mengsu, Y & Moore, M.R. (2003). In; Molluscan Shellfish Safety eds. Villalba, A., Reguera, B., Romalde, J.L. & Beiras, R.Conselleria de Pesca e Asuntos Maritimos da Xunta de Galicia and Intergovernmental Oceanographic commission of UNESCO 97-105 (ISBN 84-453 3638X) .
- ENVIRONMENTAL TOXICOLOGY OF METALS & METALLOIDS. Eds. J.C. Ng & M.R. Moore. Toxicology Letters, **137** 1-134 2003
- BIOAVAILABILITY OF METALS AND ARSENIC AT CONTAMINATED SITES FROM CATTLE DIPS, MINED LAND AND NATURALLY OCCURRING MINERALISATION ORIGINS Ng, J., Noller, B., Bruce, S., Moore, M.R. 2003 Proceedings of 5<sup>th</sup> National Workshop on the Assessment of Site Contamination eds. Langley, A., Gibley, M., and Kennedy, B. EPHC & NEPC Adelaide pp. 163- 181 (ISBN 0-642-32355-0)
- NATIONAL DIOXINS PROGRAM. Determination of ambient levels of Dioxins in Australia. Determination of the levels of Dioxins in the Australian Population. Risk assessment of Dioxin Exposure. Reports by CSIRO and EnTox to Environment Australia (Department of Environment and Heritage) 2004
- HEALTH EFFECTS OF EXPOSURE TO ULTRAFINE PARTICULATES. Report to Environment Australia by Lidia Morawska, Zoran Ristovski and Michael R. Moore. 2004
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